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[Response declined]

12/8/96855

Effect of normoxic cardiopulmonary bypass on leukocyte elastase release

To the Editor:

We read with great interest the recent paper by Ihnken and coworkers[1] about the reduction of oxygen-derived free radicals and nitric oxide by normoxic cardiopulmonary bypass (CPB). In their article, the authors showed that normoxic CPB reduced release of neutrophil elastase in patients undergoing cardiac operations. They wrote, "this is the first time that a Po_2-dependent elastase release on CPB is described."

Recently, we have undertaken a prospective study on 60 patients undergoing cardiac operations to compare the efficiency and safety of different membrane oxygenators. A large variation in Po_2 appeared during perfusion, which gave us an opportunity to assess whether elastase release during CPB was dependent on the level of Po_2. During CPB, arterial Po_2 was measured 5 times: at the start of cooling, during cooling down to 32°C, on stabilized hypothermia at 28°C, during rewarming to 32°C, and at the end of CPB. Elastase was measured before and at the end of CPB from blood samples taken from the radial artery using the same method that Ihnken and associates described (enzyme-linked immunosorbent assay; Merck, Darmstadt, Germany). Results showed that Po_2 varied between 107 and 440 mm Hg at the start of cooling and between 80 and 308 mm Hg on stabilized hypothermia during CPB. On an average of the 5 time points during CPB, Po_2 varied between 128 and 317 mm Hg. Elastase increased in the majority of patients at the end of CPB with a concentration ranging between 41 to 490 ng/mL, or a percentage increase (release) of 47% to 742% compared with baseline concentration before CPB. However, there was no correlation either between Po_2 and elastase concentration at the end of CPB or between Po_2 and the percentage increase compared with the baseline elastase (Fig 1).

Our results suggest that systemic elastase release during CPB is not dependent on Po_2. For years, elastase release during CPB has been known to be largely attributed to blood interaction with the artificial surface of the extracorporeal circuit.[2,3] Modification of the material surface of the circuit has been associated with a reduction in elastase release either during clinical CPB[4] or in a simulated model of CPB.[5] It could well be that normoxic CPB had reduced the cardiac source of elastase but that the effect had been systematically counteracted by other factors, such as blood-material interaction. Thus whether Po_2 plays a role in controlling local or systemic elastase release is of interest, but needs to be confirmed by later studies as normoxic CPB becomes more prevalent than hyperoxic CPB.

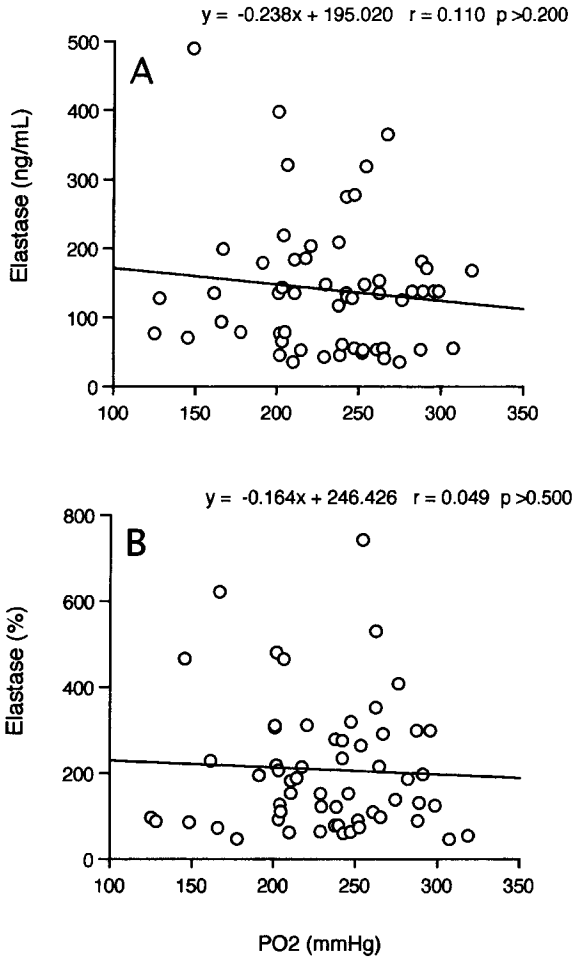

Fig 1. Scattergrams showing no relationship between arterial Po_2 and systemic elastase concentration determined at the end of CPB **(A)** or the percentage increase at the end of CPB compared with the baseline elastase **(B).** Po_2 is the average of 5 blood gas samples determined during CPB (see text for details).

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Reply to the Editor

We thank Dr Gu and his colleagues for their interest in our recent article.[1] They describe a prospective study in 60 patients in whom cardiopulmonary bypass (CPB) was used, but did not mention where these results have been published. They did not find a correlation between Po_2 on CPB and neutrophil elastase release. However, there are several methodologic differences between our two studies. First, they wrote, "a large variation in Po_2 appeared during perfusion," and their results showed that Po_2 varied between 107 and 440 mm Hg at the start of cooling, between 80 and 308 mm Hg during hypothermia, and between 128 and 317 mm Hg on average during CPB. It is not clear whether these disparities in Po_2 occurred randomly and within the same patient. Further, it is not evident whether normoxia was maintained at all times, as it was done in our study. This seems very important, because we also did not find a positive correlation between Po_2 and elastase at the beginning of CPB with low elastase levels, but when Po_2 was controlled to normoxic levels during the whole period of extracorporeal circulation, elastase release was reduced significantly compared with high levels after persistent hyperoxia. Second, they measured Po_2 levels only 5 times during CPB: Po_2 between these measurements is unknown and might have reached undesired levels. In our study, on-line Po_2 measurements were applied and the Po_2 during CPB was controlled at all times. Third, different types of oxygenators were used during their study. These differences might have influenced results, as our data (unpublished) indicate, namely, that elastase release varies between oxygenators. Fourth, blood samples in their study were obtained from the radial artery, whereas our blood samples were taken from coronary sinus blood and from the venous side of the CPB circuit. The significance of this detail, and whether this might have influenced results, however, remains unknown.

The authors mention that "elastase release during CPB has been known to be largely attributed to blood interaction with the artificial surface of the extracorporeal circuit."[2,3] These results confirm (as mentioned above) our own findings, in which membrane oxygenators cause less oxidative damage than bubble oxygenators. In their explanation, the authors reason: "It could well be that normoxic CPB had reduced the cardiac source of elastase but that the effect had been systematically counteracted by other factors, such as blood-material interaction." This statement is in contrast to our findings, in which values from coronary sinus blood and systemic circulation were not different and improved after normoxia. Independently from reduced leukocyte elastase levels, there are additional benefits from normoxic CPB.[4,5]

In summary, there are considerable methodologic differences between their study and ours. Our protocol of controlled normoxic CPB for the first time establishes a correlation between Po_2 and leukocyte elastase, whereas their investigation of "a large variation in Po_2" could not confirm this finding. I do agree with their conclusion that further studies are necessary to address this issue. Furthermore, the clinical significance of reduced leukocyte elastase after normoxic CPB has to be established.

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The extracardiac Fontan procedure using a pedicled pericardial roll without cardiopulmonary bypass

To the Editor:

We congratulate Okabe and his colleagues for their successful establishment of total cavopulmonary connection using a pedicled autologous pericardial roll without the aid of cardiopulmonary bypass.[1] We[2] used similar surgical maneu-